Effects of Lifestyle Intervention of Maternal Gestational Diabetes Mellitus on Offspring Growth Pattern Before Two Years of Age

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Our group conducted a population-based randomized controlled trial (RCT) in Tianjin, China, which tested the effectiveness of intensive care (IC) versus usual care (UC) on adverse pregnancy outcomes among women with gestational diabetes mellitus (GDM), and found that with IC of GDM during pregnancy a 98-g birth weight reduction and a 34% risk reduction in macrosomia were achieved (1). We further followed offspring born to women enrolled in the RCT from 1 month to 2 years after delivery to test whether IC of GDM during pregnancy modified early-life growth of offspring born to Chinese women with GDM.

The study settings, population, and design have been previously described (1). Briefly, a total of 19,847 pregnant women were screened for GDM with a glucose challenge test between the 24th and 28th weeks of pregnancy, and 2,921 women with a glucose challenge test level ≥7.8 mmol/L underwent the standard oral glucose tolerance test. Of them, 1,440 women with GDM were identified based on the International Association of Diabetes and Pregnancy Study Group (IADPSG) criteria (2) and 706 eligible women were randomized to either IC or UC group and completed the trial. The UC included one group diabetes education session at diagnosis of GDM, while the IC included additional two individualized diabetes education sessions at the 30th and 34th gestational weeks and three group diabetes education sessions at the 27th, 29th, and 33rd gestational weeks. The detailed intervention measures have been previously published (1).

Postpartum, 706 children born to the 706 women (IC 344 vs. UC 362) were invited to participate in the follow-up study, and 671 children (IC 324 vs. UC 347) turned up at least once for the follow-up study (an overall follow-up rate of 95%) from 1–24 months of age. Ethics of this study were approved by the Clinical Ethics Committee of Tianjin Women and Children's Health Center, and informed written consent was obtained from all of the women (ClinicalTrials.gov, clinical trial reg. no. NCT01565564).

Statistical analysis was performed with SAS release 9.4 (SAS Institute, Cary, NC). BMI-for-age and -sex and its *Z* scores were calculated from 1 to 24 months of age and divided by age-groups: 1–3, 4–6, 7–9, 10–12, 13–18, and 19–24 months of age. Overweight was defined as BMI-for-age and -sex ≥85th percentiles according to the World Health Organization age- and sex-specific growth references (3). Overweight at one time point within 1 year of age was defined as BMI-for-age and -sex ≥85th percentiles at any one time point of 1–3, 4–6, 7–9, and 10–12 months of age, while overweight at one time point at 1–2 years of age was defined as BMI-for-age and -sex ≥85th percentiles at 13–18 and 19–24 months of age.

There were no differences in clinical characteristics of women at enrollment between the IC group ($N = 324$) and the UC group ($N = 347$) ($P > 0.10$). Although children born to the women in the IC group were more likely to be male than children born to the women in the UC group, BMI-for-age and -sex and *Z* score for BMI-for-age and -sex at 1–3, 4–6, 7–9, 10–12, and 19–24 months of age were similar between children born to the women in the IC group and children born to the women in the UC group ($P > 0.10$) (Table 1). BMI-for-age and -sex and *Z* score for BMI-for-age and -sex at 13–18 months were borderline lower

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Table 1—Characteristics of offspring at follow-up by maternal IC assignment

	UC		IC		
	N	Mean (SD) or *n* (%)	*N*	Mean (SD) or *n* (%)	*P*
Male sex, *n* (%)	347	182 (52.5)	324	196 (60.5)	0.04**
BMI-for-age and -sex, kg/m^2					
1–3 months	316	17.6 (1.7)	293	17.5 (1.5)	0.17*
4–6 months	324	18.1 (1.7)	307	18.2 (2.1)	0.75*
7–9 months	284	18.1 (1.7)	267	18.2 (2.2)	0.52*
10–12 months	319	17.5 (1.5)	289	17.8 (7.4)	0.44*
13–18 months	272	17.1 (1.6)	255	16.8 (1.4)	0.07*
19–24 months	258	16.3 (1.4)	252	16.3 (1.6)	0.70*
Z score for BMI-for-age and -sex					
1–3 months	316	0.63 (1.05)	293	0.50 (0.98)	0.15*
4–6 months	324	0.59 (1.06)	307	0.60 (1.25)	0.78*
7–9 months	284	0.46 (1.02)	267	0.47 (1.09)	0.56*
10–12 months	319	0.55 (0.96)	289	0.69 (4.15)	0.63*
13–18 months	272	0.75 (1.03)	255	0.57 (0.96)	0.07*
19–24 months	258	0.26 (1.03)	252	0.28 (1.11)	0.73*
Overweight status†, *n* (%)					
1–3 months	316	101 (32.0)	293	85 (29.0)	0.43**
4–6 months	324	101 (31.2)	307	102 (33.2)	0.58**
7–9 months	304	79 (26.0)	296	89 (30.1)	0.27**
10–12 months	319	94 (29.5)	289	80 (27.7)	0.63**
13–18 months	278	101 (36.3)	257	84 (32.7)	0.38**
19–24 months	258	72 (27.9)	252	66 (26.2)	0.66**
Overweight within 1 year of age, *n* (%)		180 (51.9)		164 (50.6)	0.75**
Overweight within 1–2 years of age, *n* (%)		124 (35.7)		110 (34.0)	0.63**
Among overweight women at prepregnancy					
Overweight within 1 year of age, *n* (%)		73 (56.6)		59 (56.7)	0.98**
Overweight within 1–2 years of age, *n* (%)		59 (45.7)		45 (43.3)	0.71**
Among normal-weight women at prepregnancy					
Overweight within 1 year of age, *n* (%)		107 (49.1)		105 (47.7)	0.78**
Overweight within 1–2 years of age, *n* (%)		65 (29.8)		65 (29.6)	0.95**

*Derived from Student *t* test or Wilcoxon two-sample test. **Derived from χ^2 test or Fisher exact test. †BMI-for-age and -sex and *Z* score for BMI-for-age and -sex in children were calculated according to the age- and sex-specific growth reference of the World Health Organization, and overweight was defined as age- and sex-specific BMI ≥85th percentile.

in the children whose mother received IC than in those born to the mothers with UC. Nevertheless, overweight rates at 1–3, 4–6, 7–9, 10–12, 13–18, and 19–24 months of age were all similar in the two groups ($P > 0.20$). Overweight rates within 1 year of age and 1–2 years of age were also comparable in the two groups (51.9% vs. 50.6%, $P = 0.75$, and 35.7% vs. 34.0%, $P = 0.63$). In addition, in the subgroup analysis by maternal BMI <24 kg/m^2 and ≥24 kg/m^2 at pregnancy, overweight rates within 1 year of age and 1–2 years of age were also similar in the two groups.

GDM predisposes the offspring to a high risk of macrosomia at birth and obesity during early and late childhood. Several RCTs demonstrated that intensive management of GDM had benefits for perinatal outcomes but did not have long-term effects on childhood obesity (4,5). Consistently, our RCT found that IC significantly reduced macrosomia but did not modify the growth of offspring born to Chinese women with GDM from 1 to 24 months of age. In conclusion, IC of GDM does not modify early-life growth in offspring of mothers with GDM. However, its long-term benefits remain to be tested in future studies.

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Data and Resource Availability. The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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